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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/419,517	10/18/1999	WAYNE H. KAESEMEYER	97-092-US-C2	1371

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EXAMINER
KIM, JENNIFER M

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/05/2002 14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/419,517	KAESEMEYER, WAYNE H.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on th cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,12,13 and 16-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,12,13 and 16-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 14, 2002 has been entered.

Applicant's request for Continued Examination (RCE), directed to Examiner Dwayne C. Jones, due to his previous experience in related cases (e.g. the parent case-U.S.Patent No. 5,968,983) is noted. However, Examiner Jones is unable to examine this case due to his current heavy workload.

Claims 1-6, 12-13, and 16-26 are presented for examination.

The amendment filed October 18, 1999 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The insertion of

"atorvastatin, cerivastatin," on page 9, line 17, after "dalvastatin" lack literal support in the specification as filed.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20, 21 and 23-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The active agents, atorvastatin and cerivastatin in claims 20, 21 and 23-26 lack literal support in the specification as filed. This is a New Matter rejection.

It is suggested to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

2. Claims 20,21 and 23-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Liao et al.(U.S.Patent No. 6,147,109) of record.

Liao et al. at the abstract, column 9, lines 10- 27(particularly lines 26 and 27), column 10, lines 19-27(particularly line 27), teach applicants method and the therapeutic mixture comprising treating a disease condition in a subject comprising administering a mixture of L-arginine and Hmg-CoA reductase (atorvastatin or cerivastatin).

Since the Applicants' disclosure of atorvastatin and cerivastatin is not taught in the parent Application serial No. 08/833842, the benefit of priority date of the parent Application does not apply in instant rejection.

Therefore Applicant's priority date of above claims is the filing date of instant Application of October 18, 1999.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,2, 5, 6, 12, 13, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morris et al.(1994).

Morris et al. teach on the abstract that the optimal salt form for a novel HMG-CoA reductase inhibitor, BMS-180431 in oral dosage form is the arginine salt.

Morris et al. also on the abstract teach that above salt selection process can be easily adopted in the drug development program and can be completed within 4 to 6 weeks.

The difference between above reference and Applicant's claimed invention is lack of illustrated example of the novel HMG-CoA reductase with arginine salt for treating a disease condition. However, the skilled artisan would be motivated to employ HMG-CoA reductase together with arginine salt for treatment of hypercholesterolemia since the HMG-CoA reductase with arginine salt form is the optimal salt form for the novel HMG-CoA reductase inhibitor, BMS-180431. The skilled artisan would be motivated with reasonable expectation of success to formulate the novel HMG-CoA reductase with arginine salt form in treatment of the disease condition since this salt selection process can be easily adopted in the drug development program for it's it well known effect as

taught by Morris et al. As to claims 16 and 17 which claim a method of stimulating NO synthase administering Applicant's active agents said method involves a mechanism of action which is inherent in the treatment of medical disease condition.

Claims 1-6, 12, 13, 16-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGovern et al.(U.S. Patent No. 5,634,895) and Igo et al.(U.S.Patent No. 5,634,895), all of record.

2. McGovern et al. on the abstract, teaches a method for preventing onset of restenosis after angioplasty employing a HMG-CoA reductase, pravastatin.

3. McGovern et al. on column 1, lines 26-40, reports that lovastatin, a HMG-CoA reductase inhibitor reduces restenosis following angioplasty.

4. Igo et al. teaches on the abstract, column 6, lines 41-44, column 7, lines 7-12, a method of treating angioplasty restenosis and **coronary blood vessels** by administering nitric oxide donor agent including L-arginine.

5. The claims differ from the cited references in claiming combination of L-arginine, and HMG-CoA reductase inhibitor, to treat a condition such as restenosis following angioplasty. To employ combinations of L-arginine and HMG-CoA reductase inhibitor to treat a condition such as restenosis following angioplasty would have been obvious because all the components are well known individually for treating restenosis following angioplasty. It would be expected that the combination of components would treat restenosis following angioplasty as well.

The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)). As to claims 16 and 17 which claim a method of stimulating NO synthase administering Applicant's active agents said method involves a mechanism of action which is inherent in the treatment of medical disease condition.

6. The therapeutic amounts of active agents to be used set forth in claims 6 and 17 and formulate prior to administration or mixed together in vivo set forth in claim 5, the route of administration set forth in claim 2, and setting a periodic indicator set forth in claim 19 are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional route of administration.

Claims 1,2,5,12, 13, 16, 17, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al.(1994), Pharmacol. Res. (1996)(U) and Bocan (U.S.Patent No.6,093,719) all of record.

7. Wang et al. teaches on the abstract, that the dietary L-arginine prevents **atherogenesis** in the coronary artery of the hypercholesterolemic rabbit.

8. The U reference teaches that cerivastatin interferes major process involved in **atherogenesis**.

9. Bocan on the abstract teaches atorvastatin alone resulting in a less **atherogenic** lipoprotein profile.

The claims differ from the cited references in claiming combination of L-arginine, and HMG-CoA reductase inhibitor, cerivastatin or atorvastatin to treat a condition such as

atherogenesis. To employ combinations of L-arginine and cerivastatin or atorvastatin to treat a condition such as atherogenesis would have been obvious because all the components are well known individually for treating atherogenesis. It would be expected that the combination of components would treat atherogenesis as well. The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)). As to claims 16 and 17 which claim a method of stimulating NO synthase administering Applicant's active agents said method involves a mechanism of action which is inherent in the treatment of medical disease condition.

10.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Response to Arguments

Applicant's arguments filed January 14, 2002 have been fully considered but they are not persuasive.

Applicant's arguments are:

1. Neither McGovern nor Igo suggests Applicant's claimed invention since Restenosis is a broad medical term that involves the reparative respose to injury after angioplasty and that the purpose provided in the art of administering a Hmg-CoA reductase inhibitor is to reduce serum cholesterol to thereby reduce platelet aggregation and the purpose of administering L-arginine is to form NO thereby reducing vasoconstriction.
2. The purpose provided in the art of administering a Hmg-CoA reductase inhibitor is to reduce serum cholesterol to thereby reduce platelet aggregation and the purpose of administering L-arginine is to form NO thereby reducing vasoconstriction. Further, Wang nor Bocan provides any motivation to combine L-arginine and a Hmg-CoA reductase inhibitor.

With regard to argument 1), regardless of the purpose or mechanism of action of each of active agents, Hmg-CoA reductase and L-arginine, the ultimate effect is the same, therefore this teaching obviates Applicant's broad treatment of Restenosis employing combination of active agents to achieve at least additive effect.

With regard to argument 2), regardless of the purposes or mechanism of action of each of the active agents, Hmg-CoA reductase and L-arginine, the ultimate effect is the same, therefore this teaching obviates Applicant's broad treatment of a disease condition i.e. atherogenesis employing the combination of active agents to achieve at least additive effect.

Mac Allister et al. and Lefer et al. are withdrawn as reference.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 703-308-2232. The examiner can normally be reached on Monday through Friday 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 703-305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Theodore J. Criares
Primary Examiner
Art Unit 1617

jmk
November 3, 2002